IN THE SPECIFICATION

Please allow entry of the substitute specification attached hereto.

IN THE DRAWINGS

Please allow entry of the substitute drawings for Figures 19 and 33 attached hereto.

REMARKS

Claims 1-263 are pending in the application.

Claims 8-11, 18, 20-21, 32-35, 44-46, 55-57, 63, 74-77, 81-82, 84, 121, 127, 131-132, 137-138, 146, 154, 164-165, 173-174, 178, 186, 190, 198-199, 208, 210, 212, 219, 221-223, 225-228, 231-232, 234-235, and 252 have been amended to insert sequence identifiers as required by 37 C.F.R. §§1.821-1.825, and to correct minor typographical errors. The subject matter of the amended claims is fully supported by the application as originally filed. No new matter has been added.

In the Office Action, the Examiner indicated that Applicants' Response filed July 6, 2001 was not fully responsive to the Office Communication mailed June 20, 2001 (Office Action, page 2). In particular, the Examiner indicated that the number and nature of the amendments to include sequence identifiers rendered it difficult to consider the application and arrange the papers for printing or copying. *Id.* The Examiner therefore required a substitute specification and substitute claims for the application in accordance with 37 C.F.R. §§1.121 and 1.821-1.825. *Id.*

As a result of this amendment, Applicants have amended Claims 8-11, 18, 20-21, 32-35, 44-46, 55-57, 63, 74-77, 81-82, 84, 121, 127, 131-132, 137-138, 146, 154, 164-165, 173-174, 178, 186, 190, 198-199, 208, 210, 212, 219, 221-223, 225-228, 231-232, 234-235, and 252 to include sequence identifiers and correct minor typographical errors. The amended claims are fully supported by the application as originally filed, and no new matter has been

added. A marked copy of the amended claims is included in the attached Appendix.

In addition, Applicants have filed herewith a substitute specification and a marked copy of the substitute specification showing the amendments to include sequence identifiers. To the substitute specification, Applicants have attached a second copy of the substitute claims. To the marked copy of the substitute specification, Applicants have attached a second copy of the marked, substitute claims. Also filed herewith are substitute drawings for Figures 19 and 33, as well as marked copies of the substitute drawings showing the amendments to include sequence identifiers.

In the Appendix, and in the attached, marked copies of the substitute specification, claims, and drawings the inserted text is shown by double underlining. This is to distinguish the underlining of the sequence identifiers from underlined text in the originally filed application. No new matter has been added to the substitute specification, claims, or drawings. Entry and consideration of the substitute specification, claims, and drawings is respectfully requested.

CONCLUSION

Applicants believe that this Amendment, taken together with the Response filed July 6, 2001, is fully responsive to the Office Communication mailed June 20, 2001. In the event that the Examiner is of the opinion that further discussion of the application would be helpful, the Examiner is hereby respectfully requested to telephone Applicants' undersigned representative at (212) 415-8742 and is assured of full cooperation in an effort to advance the prosecution of the instant application and claims to allowance.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for the timely consideration of this amendment under 37 C.F.R. §§ 1.16 and 1.17, or credit any overpayment to Deposit Account No. 13-4500, Order No. 1878-4051. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,
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Dated: October 29, 2001

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APPENDIX

CLAIMS WITH MARKINGS SHOWING AMENDMENTS MADE

1. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence which binds IR and comprises the amino acid sequence $X_1X_2X_3X_4X_5$, wherein X_1, X_2, X_4, and X_5 are aromatic amino acids, and X_3 is any polar amino acid.

2. The method according to claim 1 wherein X_1, X_2, and X_5 are selected from the group consisting of phenylalanine and tyrosine, X_3 is selected from the group consisting of aspartic acid, glutamic acid, glycine and serine, and X_4 is selected from group consisting of tryptophan, tyrosine and phenylalanine.

3. The method according to claim 2 wherein said amino acid sequence is an insulin agonist.

4. The method according to claim 2 wherein said amino acid sequence is an insulin antagonist.

5. The method according to claim either one of claims 3 or 4 wherein X_1 and X_5 are phenylalanine and X_2 is tyrosine.

6. The method according to claim 5 wherein X_4 is tryptophan.

7. The method according to claim 6 wherein the amino acid sequence is an insulin agonist and X_3 is selected from the group consisting of aspartic acid and glutamic acid.

8. (Once Amended) The method according to claim 7 wherein X_3 is aspartic acid to result in an amino acid sequence comprising FYDWF (SEQ ID NO: 2411).

9. (Once Amended) The method according to claim 7 wherein X_3 is glutamic acid to result in an amino acid sequence comprising FYEWF (SEQ ID NO: 2412).

10. (Once Amended) The method according to claim 1 wherein the amino acid sequence FHEN (SEQ ID NO: 2633) is bound to the amino terminal of $X_1X_2X_3X_4X_5$ to produce an amino acid sequence comprising $FHENX_1X_2X_3X_4X_5$ (SEQ ID NO: 2634) and possessing insulin agonist activity.

11. (Once Amended) The method according to claim 10 wherein the amino acid sequence is FHENFYDWF (SEQ ID NO: 2635).

12. The method according to claim 1 wherein the amino acid sequence $X_1X_2X_3X_4X_5$ further comprises the amino acid sequence X_{93} X_{94} X_{95} X_{96} X_{97} located at the carboxy terminal end adjacent to X_5, wherein X_{93}, X_{94} and X_{97} may be any amino acid, X_{95} is selected from the group consisting of glutamine, glutamic acid, alanine and lysine, and X_{96} is a hydrophobic or aliphatic amino acid.

13. The method according to claim 12 wherein X_{93} is selected from the group consisting of alanine, aspartic acid, glutamic acid, arginine, and valine, X_{95} is glutamine or glutamic acid, and X_{96} is selected from the group consisting of leucine, isoleucine, valine and tryptophan.

14. The method according to claim 13 wherein X_{96} is leucine or tryptophan.

15. The method according to claim 14 wherein X_{96} is leucine.

16. The method according to claim 13 wherein X_{95} is glutamine or glutamic acid, and X_{96} is tryptophan.

17. The method according to claim 13 wherein X_{95} is glutamic acid and the amino acid sequence is an insulin agonist.

18. (Once Amended) The method according to claim 13 wherein asparagine is present as the amino acid bound to the amino terminal of X_1 and wherein $X_1X_2X_3X_4X_5X_{93}$ is FYDWFV (SEQ ID NO: 2636).

19. The method according to claim 1 wherein the amino acid sequence is selected from the group of amino acid sequences listed in Figures 1, 2, and 9.

20. (Once Amended) The method according to claim 1 wherein the sequence is selected from the group consisting of FHENFYDWFVRQVSK (SEQ ID NO: 2115), DYKDVTFTSAVFHENFYDWFVRQVSKK (SEQ ID NO: 2111), GRVDWLQRNANFYDWFVAELG (SEQ ID NO: 2163) and APTFYAWFNQQT (SEQ ID NO: 1870).

21. (Once Amended) The method according to claim 1 wherein the sequence is selected from the group consisting of

FHENFYDWFVRQVAKK-NH_2 (SEQ ID NO: 2447)
FHENFYDWFVRQASKK-NH_2 (SEQ ID NO: 2448)
FHENFYDWFVRAVSKK-NH_2 (SEQ ID NO: 2449)
FHENFYDWFVAQVSKK-NH_2 (SEQ ID NO: 2450)
FHENFYDWFARQVSKK-NH_2 (SEQ ID NO: 2451)
FHEAFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2452)
FHANFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2453)

FAENFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2454)
AHENFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2455)
fhenfydwfvrqvskk (SEQ ID NO: 2456)
EFHENFYDWFVRQVSEE (SEQ ID NO: 2457)
FHENFYGWFVRQVSKK (SEQ ID NO: 2458)
HETFYSMIRSLAK (SEQ ID NO: 2459)
SDGFYNAIELLS (SEQ ID NO: 2460)
SLNFYDALQLLAKK (SEQ ID NO: 2461)
HDPFYSMMKSLLK (SEQ ID NO: 2462)
NSFYEALRMLSSK (SEQ ID NO: 2463)
HPTSKEIYAKLLK (SEQ ID NO: 2464)
HPSTNQMLMKLFK (SEQ ID NO: 2465)
HPPLSELKLFLIKK (SEQ ID NO: 2466)
HAPLSVLVQALLKK (SEQ ID NO: 2467)
HPSLSDMRWILLK (SEQ ID NO: 2468)
WSDFYSYFQGLD (SEQ ID NO: 2469)
D117-Dap(D117) (SEQ ID NO: 2470)
SSNFYQALMLLS (SEQ ID NO: 2471)
D117-Dap(CO-CH_2-O-NH_2) (SEQ ID NO: 2472)
HENFYGWFVRQVSKK (SEQ ID NO: 2473)
D117-Lys(D117) (SEQ ID NO: 2474)
D117-b-Ala-Lys(D117) (SEQ ID NO: 2475)
D117-b-Ala-Dap(b-Ala-D117) (SEQ ID NO: 2476)
D117-Gly-Lys(Gly-D117) (SEQ ID NO: 2477)
D117-b-Ala-Lys(b-Ala-D117) (SEQ ID NO: 2478)
D117-Dab(D117) (SEQ ID NO: 2479)
D117-Orn(D117) (SEQ ID NO: 2480)
D117-Dap(b-Ala-D117) (SEQ ID NO: 2481)
D117-b-Ala-Orn(b-Ala-D117) (SEQ ID NO: 2482)
1-(Thia-b-Ala-D117)$_2$ (SEQ ID NO: 2483)
FHENFYDWFVRQVS (SEQ ID NO: 2484)
FHENFYDWFVRQVSK (SEQ ID NO: 2485)
FHENFYDWFVQVSK (SEQ ID NO: 2486)
FHENFYDWFVVSK (SEQ ID NO: 2487)
FHENFYDWFVSK (SEQ ID NO: 2488)
FHENFYDWFVK (SEQ ID NO: 2489)
FYDWF-NH_2 (SEQ ID NO: 2490)
FYDWFKK-NH_2 (SEQ ID NO: 2491)
AFYDWFAKK-NH_2 (SEQ ID NO: 2160)
AAAAFYDWFAAAAAKK-NH_2 (SEQ ID NO: 2492)

$(D117)_2$-12 (SEQ ID NO: 2493)
$(Cys\text{-}Gly\text{-}D117)_2$ (SEQ ID NO: 2494)
Cys-Gly-D117 (SEQ ID NO: 2495)
$(D117)_2$-14 (SEQ ID NO: 2496)
LDALDRLMRYFEERPSL-NH_2 (SEQ ID NO: 2461)
PLAELWAYFEHSEQGRSSAH-NH_2 (SEQ ID NO: 2462)
GRVDWLQRNANFYDWFVAELG-NH_2 (SEQ ID NO: 2463)
NGVERAGTGDNFYDWFVAQLH-NH_2 (SEQ ID NO: 2464)
EHWNTVDPFYFTLFEWLRESG-NH_2 (SEQ ID NO: 2465)
EHWNTVDPFYQYFSELLRESG-NH_2 (SEQ ID NO: 2466)
QSDSGTVHDRFYGWFRDTWAS-NH_2 (SEQ ID NO: 2467)
AFYDWFAK-NH_2 (SEQ ID NO: 2497)
AFYDWFA-NH_2 (SEQ ID NO: 2498)
AFYDWF-NH_2 (SEQ ID NO: 2499)
FYDWDA-NH_2 (SEQ ID NO: 2500)
Ac-FYDWF-NH_2 (SEQ ID NO: 2501)
Lig-FHENFYDWFVRQVSKK (SEQ ID NO: 2502)
Lig-GGGFHENFYDWFVRQVSKK (SEQ ID NO: 2503)
FHENFYDWFVRQVSKKGGG-Lig (SEQ ID NO: 2504)
Lig-CAWPTYWNCG (SEQ ID NO: 2505)
ACAWPTYWNCG-Lig (SEQ ID NO: 2506)
ACAWPTYWNCGGGG-Lig (SEQ ID NO: 2507)
Lig-SDGFYNAIELLS (SEQ ID NO: 2508)
SDGFYNAIELLS-Lig (SEQ ID NO: 2509)
SDGFYNAIELLSGGG-Lig (SEQ ID NO: 2510)
KHLCVLEELFWGASLFGYCSGKK-Lig (SEQ ID NO: 2511)
AFYDWFAKK-Lig (SEQ ID NO: 2512)
AFYEWFAKK-NH_2 (SEQ ID NO: 2513)
AFYGWFAKK-NH_2 (SEQ ID NO: 2514)
AFYKWFAKK-NH_2 (SEQ ID NO: 2515)
$(SDGFYNAIELLS\text{-}Lig)_2$-14 (SEQ ID NO: 2516)
$(AFYDWFAKK\text{-}Lig)_2$-14 (SEQ ID NO: 2517)
FHENAYDWFVRQVSKK (SEQ ID NO: 2518)
FHENFADWFVRQVSKK (SEQ ID NO: 2519)
FHENFYAWFVRQVSKK (SEQ ID NO: 2520)
FHENFYDAFVRQVSKK (SEQ ID NO: 2521)
FHENFTDWAVRQVSKK (SEQ ID NO: 2522)
FQSLLEELVWGAPLFRYGTG (SEQ ID NO: 2523)
PLCVLEELFWGASLFGQCSG (SEQ ID NO: 2524)
QLEEEWAGVQCEVYGRECPS (SEQ ID NO: 2525)

Cys-$(Gly)_2$-D117 (SEQ ID NO: 2526)
$(Cys\text{-}(Gly)_2\text{-}D117)_2$ (SEQ ID NO: 2527)
(S210)-14-(S212) (SEQ ID NO: 2528)
(S131)-14-(S212) (SEQ ID NO: 2529)
$(S205)_2$-14 (SEQ ID NO: 2530)
$(S204)_2$-14 (SEQ ID NO: 2531)
(S131)-14-(S210) (SEQ ID NO: 2532)
RVDWLQRNANFYDWFVAELG (SEQ ID NO: 2533)
VDWLQRNANFYDWFVAELG (SEQ ID NO: 2534)
DWLQRNANFYDWFVAELG (SEQ ID NO: 2535)
WLQRNANFYDWFVAELG (SEQ ID NO: 2536)
LQRNANFYDWFVAELG (SEQ ID NO: 2537)
QRNANFYDWFVAELG (SEQ ID NO: 2538)
RNANFYDWFVAELG (SEQ ID NO: 2539)
NANFYDWFVAELG (SEQ ID NO: 2540)
ANFYDWFVAELG (SEQ ID NO: 2541)
NFYDWFVAELG (SEQ ID NO: 2542)
GRVDWLQRNANFYDWFVAELG-Lig (SEQ ID NO: 2543)
Lig-GRVDWLQRNANFYDWFVAELG (SEQ ID NO: 2544)
(S208)-14-(S131) (SEQ ID NO: 2545)
(S208)-14-(S209) (SEQ ID NO: 2546)
GRVDWLQRNANFYDWFVAEL (SEQ ID NO: 2547)
GRVDWLQRNANFYDWFVAE (SEQ ID NO: 2548)
GRVDWLQRNANFYDWFVA (SEQ ID NO: 2549)
GRVDWLQRNANFYDWFV (SEQ ID NO: 2550)
14-$(SDGFYNAIELLS\text{-}Lig)_2$ (SEQ ID NO: 2551)
(GRVDWLQRNANFYDWFVAELG)-14 (SEQ ID NO: 2552)
14-(GRVDWLQRNANFYDWFVAE LG) (SEQ ID NO: 2553)
$(SDGFYNAIELLSGGG)_2$-14 (SEQ ID NO: 2554)
H-**Acy**-CLEE-**w**-GASL-**Tic**-QCSG-NH_2 (SEQ ID NO: 2555)
RWPNFYGYFESLLTHFS-NH_2 (SEQ ID NO: 2172)
HYNAFYEYFQVLLAETW-NH_2 (SEQ ID NO: 2173)
EGWDFYSYFSGLLASVT-NH_2 (SEQ ID NO: 2174)
LDRQFYRYFQDLLVGFM-NH_2 (SEQ ID NO: 2556)
WGRSFYRYFETLLAQGI-NH_2 (SEQ ID NO: 2557)
PLCFLQELFGGASLGGYCSG-NH_2 (SEQ ID NO: 2558)
WLEQERAWIWCEIQGSGCRA-NH_2 (SEQ ID NO: 2559)
IQGWEPFYGWFDDVVAQMFEE-NH_2 (SEQ ID NO: 2171)
TGHRLGLDEQFYWWFRDALSG-NH_2 (SEQ ID NO: 2560)
H-**Abu**-CLEE-**w**-GASL-**Tic**-QCSG-NH_2 (SEQ ID NO: 2561)

14-(Dap-CAWPTYWNCG)$_2$ (SEQ ID NO: 2562)
RDHypFYDWFDDi-NH2 (SEQ ID NO: 2563)
S131-14-S209 (SEQ ID NO: 2564)
S294-14-S210 (SEQ ID NO: 2565)
S295-14-S210 (SEQ ID NO: 2566)
S294-14-204 (SEQ ID NO: 2567)
S295-14-S204 (SEQ ID NO: 2568)
GFREGQRWYWFVAQVT-NH_2 (SEQ ID NO: 246)
VASGHVLHGQFYRWFVDQFALEE-NH_2 (SEQ ID NO: 2569)
VGDFCVSHDCFYGWFLRESMQ-NH_2 (SEQ ID NO: 2570)
DLRVLCELFGGAYVLGYCSE-NH_2 (SEQ ID NO: 2571)
HLSVGEELSWWVALLGQWAR-NH_2 (SEQ ID NO: 2572)
APVSTEELRWGALLFGQWAG-NH_2 (SEQ ID NO: 2573)
ALEEEWAWVQVRSIRSGLPL-NH_2 (SEQ ID NO: 2574)
WLEHEWAQIQCELYGRGCTY-NH_2 (SEQ ID NO: 2575)
AAVHEQFYDWFADQYEE-NH_2 (SEQ ID NO: 2576)
QAPSNFYDWFVREWDEE-NH_2 (SEQ ID NO: 2577)
QSFYDYIEELLGGEWKK-NH_2 (SEQ ID NO: 2578)
DPFYQGLWEWLRESGEE-NH_2 (SEQ ID NO: 2579)
$(S204)_2$-7 (SEQ ID NO: 2580)
$(S204)_2$-9 (SEQ ID NO: 2581)
$(S204)_2$-12 (SEQ ID NO: 2582)
$(S204)_2$-13 (SEQ ID NO: 2583)
DWLQRNANFYDWFVAEL-Lig (SEQ ID NO: 2584)
Lig-DWLQRNANFYDWFVAEL (SEQ ID NO: 2585)
$(S209)_2$-9 (SEQ ID NO: 2586)
$(S210)_2$-9 (SEQ ID NO: 2587)
LigKHLCVLEELFWGASLFGYCSGKKKK (SEQ ID NO: 2588)
KHLCVLEELFWGASLFGYCSGKKKK-Lig (SEQ ID NO: 2589)
$(S294)_2$-14 (SEQ ID NO: 2590)
$(S295)_2$-14 (SEQ ID NO: 2591)
S-D-G-F-Y-N-A-Acy-E-L-L-S (SEQ ID NO: 2592)
S-G-P-F-Y-E-E-Acy-E-L-L-W-Aib (SEQ ID NO: 2593)
G-G-S-F-Y-D-D-Acy-E-Aib-L-W-Aib (SEQ ID NO: 2594)
N-Aib-P-F-Y-D-E-Acy-D-E-Cha-W-Aib (SEQ ID NO: 2595)
GRVDWLQRNANFYDWFVAEAcyG-NH_2 (SEQ ID NO: 2596)
and wherein underlined numbers represent a linker as defined in Table 18.

22. The method according to claim 2 wherein the amino acid sequence binds to the insulin receptor with an affinity of at least about 10^{-5} M.

23. The method according to claim 22 wherein the affinity is at least about 10^{-7} M.

24. The method according to claim 23 wherein the affinity is at least about 10^{-9} M.

25. An amino acid sequence comprising $X_1X_2X_3X_4X_5$ wherein X_1, X_2, X_4, and X_5 are aromatic amino acids, X_3 is any polar amino acid, and wherein said amino acid sequence binds to IGF-1R.

26. The amino acid sequence according to claim 25 wherein the IGF-1R binding occurs with an affinity (K_d) of at least about 10^{-5} M.

27. The amino acid sequence according to claim 25 wherein the binding occurs at an affinity (K_d) of at least about 10^{-7} M.

28. The amino acid sequence according to claim 25 wherein X_1, X_2, and X_5 are selected from the group consisting of phenylalanine and tyrosine, X_3 is selected from the group consisting of aspartic acid, glutamic acid, glycine and serine, and X_4 is selected from group consisting of tryptohpan, tyrosine and phyenylalanine.

29. The amino acid sequence according to claim 28 wherein X_3 is selected from the group consisting of aspartic acid and glutamic acid.

30. The amino acid sequence according to claim 29 wherein X_1 and X_5 are phyenylalanine and X_2 is tyrosine.

31. The amino acid sequence according to claim 29 wherein X_4 is tryptophan.

32. (Once Amended) The amino acid sequence according to claim 31 wherein X_3 is aspartic acid to result in an amino acid sequence comprising FYDWF (SEQ ID NO: 2411).

33. (Once Amended) The amino acid sequence according to claim 31 wherein X_3 is glutamic acid to result in an amino acid sequence comprising FYEWF (SEQ ID NO: 2412).

34. (Once Amended) The amino acid sequence according to claim 28 wherein the amino acid sequence FHEN (SEQ ID NO: 2633) is bound to the amino terminal of $X_1X_2X_3X_4X_5$ to produce an amino acid sequence comprising $FHENX_1X_2X_3X_4X_5$ (SEQ ID NO: 2634).

35. (Once Amended) The amino acid sequence according to claim 34 wherein the amino acid sequence comprises FHENFYDWF (SEQ ID NO: 2635).

36. The amino acid sequence according to claim 25 wherein the amino acid sequence $X_1X_2X_3X_4X_5$ further comprises the amino acid sequence X_{93} X_{94} X_{95} X_{96} X_{97} located at the carboxy terminal end adjacent to X_5 to form $X_1X_2X_3X_4X_5X_{93}X_{94}X_{95}X_{96}X_{97}$, wherein X_{93}, X_{94} and X_{97} may be any amino acid, X_{95} is selected from the group consisting of glutamine, glutamic acid, alanine and lysine, and X_{96} is a hydrophobic or aliphatic amino acid.

37. The amino acid sequence according to claim 36 wherein X_{93} is selected from the group consisting of alanine, aspartic acid, glutamic acid, arginine, and valine, X_{95} is glutamine or glutamic acid, and X_{96} is selected from the group consisting of leucine, isoleucine, valine and tryptophan.

38. The amino acid sequence according to claim 37 wherein X_{96} is leucine or tryptophan.

39. The amino acid sequence according to claim 38 wherein X_{96} is leucine.

40. The amino acid sequence according to claim 39 wherein X_{95} is glutamine, and X_{96} is tryptophan.

41. The amino acid sequence according to claim 40 wherein X_{93} is valine.

42. The amino acid sequence according to claim 41 wherein asparagine is bound to the amino terminal of X_1.

43. An amino acid sequence selected from the amino acid sequences listed in Figures 1-A through 1-O.

44. (Once Amended) The amino acid sequence according to claim 25 wherein the sequence is selected from the group consisting of FHENFYDWFVRQVS (SEQ ID NO: 2115), DYKDVTFTSAVFHENFYDWFVRQVSKK (SEQ ID NO: 2111), GRVDWLQRNANFYDWFVAELG (SEQ ID NO: 2163) and APTFYAWFNQQT (SEQ ID NO: 1870).

45. (Once Amended) The amino acid sequence according to claim 25 wherein the sequence comprises FHENFYDWFVRQVS (SEQ ID NO: 2115).

46. (Once Amended) The amino acid sequence according to claim 25 wherein the sequence is selected from the group consisting of

FHENFYDWFVRQVAKK-NH_2 (SEQ ID NO: 2447)
FHENFYDWFVRQASKK-NH_2 (SEQ ID NO: 2448)
FHENFYDWFVRAVSKK-NH_2 (SEQ ID NO: 2449)
FHENFYDWFVAQVSKK-NH_2 (SEQ ID NO: 2450)
FHENFYDWFARQVSKK-NH_2 (SEQ ID NO: 2451)
FHEAFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2452)
FHANFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2453)
FAENFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2454)
AHENFYDWFVRQVSKK-NH_2 (SEQ ID NO: 2455)
fhenfydwfvrqvskk (SEQ ID NO: 2456)
EFHENFYDWFVRQVSEE (SEQ ID NO: 2457)
FHENFYGWFVRQVSKK (SEQ ID NO: 2458)
HETFYSMIRSLAK (SEQ ID NO: 2459)
SDGFYNAIELLS (SEQ ID NO: 2460)
SLNFYDALQLLAKK (SEQ ID NO: 2461)
HDPFYSMMKSLLK (SEQ ID NO: 2462)
NSFYEALRMLSSK (SEQ ID NO: 2463)
HPTSKEIYAKLLK (SEQ ID NO: 2464)
HPSTNQMLMKLFK (SEQ ID NO: 2465)
HPPLSELKLFLIKK (SEQ ID NO: 2466)
HAPLSVLVQALLKK (SEQ ID NO: 2467)
HPSLSDMRWILLK (SEQ ID NO: 2468)
WSDFYSYFQGLD (SEQ ID NO: 2469)
D117-Dap(D117) (SEQ ID NO: 2470)
SSNFYQALMLLS (SEQ ID NO: 2471)
D117-Dap(CO-CH_2-O-NH_2) (SEQ ID NO: 2472)
HENFYGWFVRQVSKK (SEQ ID NO: 2473)
D117-Lys(D117) (SEQ ID NO: 2474)
D117-b-Ala-Lys(D117) (SEQ ID NO: 2475)
D117-b-Ala-Dap(b-Ala-D117) (SEQ ID NO: 2476)
D117-Gly-Lys(Gly-D117) (SEQ ID NO: 2477)
D117-b-Ala-Lys(b-Ala-D117) (SEQ ID NO: 2478)
D117-Dab(D117) (SEQ ID NO: 2479)

D117-Orn(D117) (SEQ ID NO: 2480)
D117-Dap(b-Ala-D117) (SEQ ID NO: 2481)
D117-b-Ala-Orn(b-Ala-D117) (SEQ ID NO: 2482)
1-(Thia-b-Ala-D117)$_2$ (SEQ ID NO: 2483)
FHENFYDWFVRQVS (SEQ ID NO: 2484)
FHENFYDWFVRQVSK (SEQ ID NO: 2485)
FHENFYDWFVQVSK (SEQ ID NO: 2486)
FHENFYDWFVVSK (SEQ ID NO: 2487)
FHENFYDWFVSK (SEQ ID NO: 2488)
FHENFYDWFVK (SEQ ID NO: 2489)
FYDWF-NH_2 (SEQ ID NO: 2490)
FYDWFKK-NH_2 (SEQ ID NO: 2491)
AFYDWFAKK-NH_2 (SEQ ID NO: 2160)
AAAAFYDWFAAAAAKK-NH_2 (SEQ ID NO: 2492)
(D117)$_2$-12 (SEQ ID NO: 2493)
(Cys-Gly-D117)$_2$ (SEQ ID NO: 2494)
Cys-Gly-D117 (SEQ ID NO: 2495)
(D117)$_2$-14 (SEQ ID NO: 2496)
LDALDRLMRYFEERPSL-NH_2 (SEQ ID NO: 2461)
PLAELWAYFEHSEQGRSSAH-NH_2 (SEQ ID NO: 2462)
GRVDWLQRNANFYDWFVAELG-NH_2 (SEQ ID NO: 2463)
NGVERAGTGDNFYDWFVAQLH-NH_2 (SEQ ID NO: 2464)
EHWNTVDPFYFTLFEWLRESG-NH_2 (SEQ ID NO: 2465)
EHWNTVDPFYQYFSELLRESG-NH_2 (SEQ ID NO: 2466)
QSDSGTVHDRFYGWFRDTWAS-NH_2 (SEQ ID NO: 2467)
AFYDWFAK-NH_2 (SEQ ID NO: 2497)
AFYDWFA-NH_2 (SEQ ID NO: 2498)
AFYDWF-NH_2 (SEQ ID NO: 2499)
FYDWDA-NH_2 (SEQ ID NO: 2500)
Ac-FYDWF-NH_2 (SEQ ID NO: 2501)
Lig-FHENFYDWFVRQVSKK (SEQ ID NO: 2502)
Lig-GGGFHENFYDWFVRQVSKK (SEQ ID NO: 2503)
FHENFYDWFVRQVSKKGGG-Lig (SEQ ID NO: 2504)
Lig-CAWPTYWNCG (SEQ ID NO: 2505)
ACAWPTYWNCG-Lig (SEQ ID NO: 2506)
ACAWPTYWNCGGGG-Lig (SEQ ID NO: 2507)
Lig-SDGFYNAIELLS (SEQ ID NO: 2508)
SDGFYNAIELLS-Lig (SEQ ID NO: 2509)
SDGFYNAIELLSGGG-Lig (SEQ ID NO: 2510)
KHLCVLEELFWGASLFGYCSGKK-Lig (SEQ ID NO: 2511)

AFYDWFAKK-Lig (SEQ ID NO: 2512)
AFYEWFAKK-NH_2 (SEQ ID NO: 2513)
AFYGWFAKK-NH_2 (SEQ ID NO: 2514)
AFYKWFAKK-NH_2 (SEQ ID NO: 2515)
$(SDGFYNAIELLS\text{-}Lig)_2$-14 (SEQ ID NO: 2516)
$(AFYDWFAKK\text{-}Lig)_2$-14 (SEQ ID NO: 2517)
FHENAYDWFVRQVSKK (SEQ ID NO: 2518)
FHENFADWFVRQVSKK (SEQ ID NO: 2519)
FHENFYAWFVRQVSKK (SEQ ID NO: 2520)
FHENFYDAFVRQVSKK (SEQ ID NO: 2521)
FHENFTDWAVRQVSKK (SEQ ID NO: 2522)
FQSLLEELVWGAPLFRYGTG (SEQ ID NO:2523)
PLCVLEELFWGASLFGQCSG (SEQ ID NO: 2524)
QLEEEWAGVQCEVYGRECPS (SEQ ID NO: 2525)
Cys-$(Gly)_2$-D117 (SEQ ID NO: 2526)
$(Cys\text{-}(Gly)_2\text{-}D117)_2$ (SEQ ID NO: 2527)
(S210)-14-(S212) (SEQ ID NO: 2528)
(S131)-14-(S212) (SEQ ID NO: 2529)
$(S205)_2$-14 (SEQ ID NO: 2530)
$(S204)_2$-14 (SEQ ID NO: 2531)
(S131)-14-(S210) (SEQ ID NO: 2532)
RVDWLQRNANFYDWFVAELG (SEQ ID NO: 2533)
VDWLQRNANFYDWFVAELG (SEQ ID NO: 2534)
DWLQRNANFYDWFVAELG (SEQ ID NO: 2535)
WLQRNANFYDWFVAELG (SEQ ID NO: 2536)
LQRNANFYDWFVAELG (SEQ ID NO: 2537)
QRNANFYDWFVAELG (SEQ ID NO: 2538)
RNANFYDWFVAELG (SEQ ID NO: 2539)
NANFYDWFVAELG (SEQ ID NO: 2540)
ANFYDWFVAELG (SEQ ID NO: 2541)
NFYDWFVAELG (SEQ ID NO: 2542)
GRVDWLQRNANFYDWFVAELG-Lig (SEQ ID NO: 2543)
Lig-GRVDWLQRNANFYDWFVAELG (SEQ ID NO: 2544)
(S208)-14-(S131) (SEQ ID NO: 2545)
(S208)-14-(S209) (SEQ ID NO: 2546)
GRVDWLQRNANFYDWFVAEL (SEQ ID NO: 2547)
GRVDWLQRNANFYDWFVAE (SEQ ID NO: 2548)
GRVDWLQRNANFYDWFVA (SEQ ID NO: 2549)
GRVDWLQRNANFYDWFV (SEQ ID NO: 2550)
14-$(SDGFYNAIELLS\text{-}Lig)_2$ (SEQ ID NO: 2551)

(GRVDWLQRNANFYDWFVAELG)-14 (SEQ ID NO: 2552)
14-(GRVDWLQRNANFYDWFVAE LG) (SEQ ID NO: 2553)
$(SDGFYNAIELLSGGG)_2$-14 (SEQ ID NO: 2554)
H-**Acy**-CLEE-**w**-GASL-**Tic**-QCSG-NH_2 (SEQ ID NO: 2555)
RWPNFYGYFESLLTHFS-NH_2 (SEQ ID NO: 2172)
HYNAFYEYFQVLLAETW-NH_2 (SEQ ID NO: 2173)
EGWDFYSYFSGLLASVT-NH_2 (SEQ ID NO: 2174)
LDRQFYRYFQDLLVGFM-NH_2 (SEQ ID NO: 2556)
WGRSFYRYFETLLAQGI-NH_2 (SEQ ID NO: 2557)
PLCFLQELFGGASLGGYCSG-NH_2 (SEQ ID NO: 2558)
WLEQERAWIWCEIQGSGCRA-NH_2 (SEQ ID NO: 2559)
IQGWEPFYGWFDDVVAQMFEE-NH_2 (SEQ ID NO: 2171)
TGHRLGLDEQFYWWFRDALSG-NH_2 (SEQ ID NO: 2560)
H-**Abu**-CLEE-**w**-GASL-**Tic**-QCSG-NH_2 (SEQ ID NO: 2561)
14-$(Dap\text{-}CAWPTYWNCG)_2$ (SEQ ID NO: 2562)
RDHypFYDWFDDi-NH2 (SEQ ID NO: 2563)
S131-14-S209 (SEQ ID NO: 2564)
S294-14-S210 (SEQ ID NO: 2565)
S295-14-S210 (SEQ ID NO: 2566)
S294-14-204 (SEQ ID NO: 2567)
S295-14-S204 (SEQ ID NO: 2568)
GFREGQRWYWFVAQVT-NH_2 (SEQ ID NO: 246)
VASGHVLHGQFYRWFVDQFALEE-NH_2 (SEQ ID NO: 2569)
VGDFCVSHDCFYGWFLRESMQ-NH_2 (SEQ ID NO: 2570)
DLRVLCELFGGAYVLGYCSE-NH_2 (SEQ ID NO: 2571)
HLSVGEELSWWVALLGQWAR-NH_2 (SEQ ID NO: 2572)
APVSTEELRWGALLFGQWAG-NH_2 (SEQ ID NO: 2573)
ALEEEWAWVQVRSIRSGLPL-NH_2 (SEQ ID NO: 2574)
WLEHEWAQIQCELYGRGCTY-NH_2 (SEQ ID NO: 2575)
AAVHEQFYDWFADQYEE-NH_2 (SEQ ID NO: 2576)
QAPSNFYDWFVREWDEE-NH_2 (SEQ ID NO: 2577)
QSFYDYIEELLGGEWKK-NH_2 (SEQ ID NO: 2578)
DPFYQGLWEWLRESGEE-NH_2 (SEQ ID NO: 2579)
$(S204)_2$-7 (SEQ ID NO: 2580)
$(S204)_2$-9 (SEQ ID NO: 2581)
$(S204)_2$-12 (SEQ ID NO: 2582)
$(S204)_2$-13 (SEQ ID NO: 2583)
DWLQRNANFYDWFVAEL-Lig (SEQ ID NO: 2584)
Lig-DWLQRNANFYDWFVAEL (SEQ ID NO: 2585)
$(S209)_2$-9 (SEQ ID NO: 2586)

$(S210)_2$-9 (SEQ ID NO: 2587)
LigKHLCVLEELFWGASLFGYCSGKKKK (SEQ ID NO: 2588)
KHLCVLEELFWGASLFGYCSGKKKK-Lig (SEQ ID NO: 2589)
$(S294)_2$-14 (SEQ ID NO: 2590)
$(S295)_2$-14 (SEQ ID NO: 2591)
S-D-G-F-Y-N-A-Acy-E-L-L-S (SEQ ID NO: 2592)
S-G-P-F-Y-E-E-Acy-E-L-L-W-Aib (SEQ ID NO: 2593)
G-G-S-F-Y-D-D-Acy-E-Aib-L-W-Aib (SEQ ID NO: 2594)
N-Aib-P-F-Y-D-E-Acy-D-E-Cha-W-Aib (SEQ ID NO: 2595)
GRVDWLQRNANFYDWFVAEAcyG-NH_2 (SEQ ID NO: 2596)
and wherein underlined numbers represent a linker as defined in Table 18.

47. An amino acid sequence which specifically binds IR such that binding to IGF-1R is at or below background and wherein said amino acid sequence comprises $X_1X_2X_3X_4X_5$ wherein X_1, X_2, and X_5 are selected from the group consisting of phenylalanine and tyrosine, X_3 is selected from the group consisting of aspartic acid, glutamic acid, glycine and serine, and X_4 is selected from group consisting of tryptohpan, tyrosine and phyenylalanine.

48. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence which binds IR and comprises the sequence of amino acids $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ wherein X_6 and X_7 are aromatic amino acids or glutamine, X_8, X_9, X_{11} and X_{12} may be any amino acid, X_{10} and X_{13} are hydrophobic amino acids.

49. The method according to claim 48 wherein X_6 and X_7 are selected from group consisting of phenylalanine and tyrosine, and X_{10} and X_{13} are selected from group consisting of leucine, isoleucine, tryptophan, phenylalanine methionine and valine.

50. The method according to claim 48 wherein X_6 is phenylalanine and X_7 is tyrosine.

51. The method according to claim 50 wherein X_{10} is isoleucine.

52. The method according to claim 50 wherein X_{10} is leucine.

53. The method according to claim 50 wherein X_{13} is leucine.

54. The method according to claim 50 wherein X_9 is tyrosine and X_{10} is phenylalanine.

55. (Once Amended) The method according to claim 50 wherein the amino acid sequence is selected from $FYX_8X_9LX_{11}X_{12}L$ (SEQ ID NO: 2416), $FYX_8X_9IX_{11}X_{12}L$ (SEQ ID NO: 2417) and $FYX_8YFX_{11}X_{12}L$ (SEQ ID NO: 2419).

56. (Once Amended) The method according to claim 55 wherein the amino acid sequence comprises $FYX_8X_9LX_{11}X_{12}L$ (SEQ ID NO: 2416).

57. (Once Amended) The method according to claim 55 wherein the amino acid sequence comprises FYX_8 $YFX_{11}X_{12}L$ (SEQ ID NO: 2419).

58. The method according to claim 48 wherein the amino acid sequence $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ further comprises amino acids X_{98} and X_{99} at the amino terminal end and X_{100} at the carboxy terminal end to form $X_{98}X_{99}X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{100}$ and wherein X_{98} is optionally aspartic acid and X_{99} is independently an amino acid selected from the group consisting of glycine, glutamine and proline, and X_{100} is a hydrophobic amino acid.

59. The method according to claim 58 wherein X_{100} is an aliphatic amino acid.

60. The method according to claim 59 wherein X_{100} is leucine.

61. The method according to claim 48 wherein the amino acid sequence binds to the insulin receptor with an affinity of at least about 10^{-5} M.

62. The method according to claim 61 wherein the affinity is between about 10^{-7} M.

63. (Once Amended) The method according to claim 48 wherein the amino acid sequence comprises DYKDFYDAIDQLVRGSARAGGTRD (SEQ ID NO: 2379) or KDRAFYNGLRDLVGAVYGAWD (SEQ ID NO: 2637).

64. The method according to claim 48 wherein the amino acid sequence is selected from the group of amino acid sequences listed in Figures 2A through 2P.

65. An amino acid sequence comprising $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ wherein X_6 and X_7 are aromatic amino acids or glutamine, X_8, X_9, X_{11} and X_{12} may be any amino acid, X_{10} and X_{13} are hydrophobic amino acids and wherein said amino acid sequence binds to IGF-1R.

66. The amino acid sequence according to claim 65 wherein the binding occurs at an affinity (K_d) of at least about 10^{-5} M.

67. The amino acid sequence according to claim 66 wherein the binding occurs at an affinity (K_d) of at least about 10^{-7} M.

68. The amino acid sequence according to claim 65 wherein X_6 and X_7 are phenylalanine or tyrosine, and X_{10} and X_{13} are leucine, isoleucine, tryptophan, phenylalanine or methionine.

69. The amino acid sequence according to claim 68 wherein X_6 is phenylalanine and X_7 is tyrosine.

70. The amino acid sequence according to claim 68 wherein X_{10} is isoleucine.

71. The amino acid sequence according to claim 68 wherein X_{10} is leucine.

72. The amino acid sequence according to claim 69 wherein X_{13} is leucine.

73. The amino acid sequence according to claim 69 wherein X_9 is tyrosine and X_{10} is phenylalanine.

74. (Once Amended) The amino acid sequence according to claim 68 wherein the amino acid sequence comprises an amino acid sequence selected from $FYX_8X_9LX_{11}X_{12}L$ (SEQ ID NO: 2416), $FYX_8X_9IX_{11}X_{12}L$ (SEQ ID NO: 2417) and $FYX_8YFX_{11}X_{12}L$ (SEQ ID NO: 2419).

75. (Once Amended) The amino acid sequence according to claim 74 wherein the amino acid sequence comprises $FYX_8X_9IX_{11}X_{12}L$ (SEQ ID NO: 2416).

76. (Once Amended) The amino acid sequence according to claim 74 wherein the amino acid sequence comprises $FYX_8X_9LX_{11}X_{12}L$ (SEQ ID NO: 2416).

77. (Once Amended) The amino acid sequence according to claim 74 wherein the amino acid sequence is $FYX_8YFX_{11}X_{12}L$ (SEQ ID NO: 2419).

78. The amino acid sequence according to claim 65 wherein the amino acid sequence $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ further comprises amino acids X_{98} and X_{99} at the amino terminal end and X_{100} at the carboxy terminal end to form $X_{98}X_{99}X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}X_{100}$ and wherein X_{98} is optionally aspartic acid and X_{99} is independently an amino acid selected from the group consisting of glycine, glutamine and proline, and X_{100} is a hydrophobic amino acid.

79. The amino acid sequence according to claim 78 wherein X_{100} is an aliphatic amino acid.

80. The amino acid sequence according to claim 79 wherein X_{100} is leucine.

81. (Once Amended) The amino acid sequence according to claim 68 wherein the amino acid sequence comprises DYKDFYDAIDQLVRGSARAGGTRD (SEQ ID NO: 2379) or KDRAFYNGLRDLVGAVYGAWDKK (SEQ ID NO: 2117).

82. (Once Amended) The sequence according to claim 81 wherein the amino acid sequence comprises DYKDFYDAIDQLVRGSARAGGTRD (SEQ ID NO: 2379).

83. An amino acid sequence comprising an amino acid sequence selected from the group consisting of amino sequences listed in Figures 2A through 2P.

84. (Once Amended) An amino acid sequence comprising a sequence selected from the group consisting of

SFYEAIHQLLGV (SEQ ID NO: 1964),
NSFYEALRMLSS (SEQ ID NO: 2638),

SLNFYDALQLLA (SEQ ID NO: 2639),
SSNFYQALMLLS (SEQ ID NO: 2471),
SDGFYNAIELLS (SEQ ID NO: 2460,
HETFYSMIRSLA (SEQ ID NO: 2640),
HDPFYSMMKSLL (SEQ ID NO: 2641) and
WSDFYSYFQGLD (SEQ ID NO: 2469).

85. (Once Amended) The amino acid sequence according to claim 65 wherein the sequence comprises the amino acid sequence $X_{115}X_{116}X_{117}X_{118}FYX_8YFX_{11}X_{12}LX_{119}X_{120}X_{121}X_{122}$ (SEQ ID NO: 2420) wherein X_{115} is selected from the group consisting of trytophan, glycine, aspartic acid, glutamic acid and arginine, X_{116} is selected from the group consisting of aspartic acid, histidine, glycine and asparagine, X_{117} and X_{118} are selected from the group consisting of glycine, aspartic acid, glutamic acid, asparagine, and alanine, X_8 is selected from the group consisting of arginine, glycine, glutamic acid and serine, X_{11} is selected from the group consisting of glutamic acid, asparagine, glutamine and tryptophan, X_{12} is selected from the group consisting of aspartic acid, glutamic acid, glycine, lysine, and glutamine, X_{119} is selected from the group consisting of glutamic acid, glycine, glutamine, aspartic acid and alanine, X_{120} is selected from the group consisting of glutamic acid, aspartic acid, glycine and glutamine, X_{121} is selected from the group consisting of tryptophan, tyrosine, glutamic acid, phenylalanine, histidine and aspartic acid, and X_{122} is selected from the group consisting of glutamic acid, aspartic acid, and glycine.

86. The amino acid sequence according to claim 85 wherein X_{115} is tryptophan, X_{117} is selected from glycine, aspartic acid, glutamic acid and asparagine; X_{118} is selected from glycine, aspartic acid, glutamic acid and alanine; X_{11}, X_{119}, X_{120}, and X_{122} are glutamic acid; X_{12} is aspartic acid, and X_{121} is tryptophan or tyrosine.

87. An amino acid sequence comprising $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ wherein X_6 and X_7 are aromatic amino acids or glutamine, X_8, X_9, X_{11} and X_{12} may be any amino acid, X_{10} and X_{13} are hydrophobic amino acids and wherein said amino acid sequence binds to IR such that binding to IGF-1R is at or below background.

88. A method of binding to Site 1 of IR from mammalian cells, said method comprising contacting IR with an amino acid sequence which binds IR and comprises the sequence of $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

89. The method according to claim 88 wherein X_{14} and X_{17} are selected from the group consisting of leucine, isoleucine and valine; X_{20} is selected from group consisting of tyrosine and histidine; and X_{21} is selected from group consisting of phenylalanine and tyrosine.

90. The method according to claim 89 wherein X_{14} and X_{17} are leucine.

91. The method according to claim 89 wherein X_{14} is leucine.

92. The method according to claim 89 wherein X_{17} is leucine.

93. The method according to claim 89 wherein X_{20} is tyrosine.

94. The method according to claim 89 wherein X_{21} is phenylalanine.

95. The method according to claim 90 wherein X_{15} is a large amino acid.

96. The method according to claim 89 wherein said amino acid sequence further comprises an amino acid extension comprising $X_{101}X_{102}X_{103}$ wherein X_{103} is bound to X_{14} at the amino terminus and X_{101} and X_{102} are polar amino acids and X_{103} is a hydrophobic amino acid.

97. The method according to claim 96 wherein X_{101} and X_{102} are independently aspartic acid or glutamic acid and X_{103} is leucine, isoleucine or valine.

98. A method of binding to Site 1 of IGF-1R from mammalian cells, said method comprising contacting IGF-1R with an amino acid sequence which binds IR and comprises the sequence of $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

99. The method according to claim 98 wherein X_{14} and X_{17} are selected from the group consisting of leucine, isoleucine and valine; X_{18} is an aromatic amino acid; X_{20} is selected from group consisting of tyrosine and histidine; and X_{21} is selected from group consisting of phenylalanine and tyrosine.

100. The method according to claim 98 wherein the amino acid sequence comprises a sequence selected from the sequences in Figures 3A through 3D.

101. An amino acid sequence which binds Site 1 of IR from mammalian cells, said sequence comprising $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

102. The amino acid sequence according to claim 101 wherein X_{14} and X_{17} are selected from the group consisting of leucine, isoleucine and valine; X_{20} is selected from group consisting of phenylalanine and tyrosine.

103. The amino acid sequence according to claim 102 wherein X_{14} and X_{17} are leucine.

104. The amino acid sequence according to claim 102 wherein X_{14} is leucine.

105. The amino acid sequence according to claim 102 wherein X_{17} is leucine.

106. The amino acid sequence according to claim 102 wherein amino acid X_{18} is tryptophan.

107. The amino acid sequence according to claim 103 wherein X_{20} is tyrosine.

108. The amino acid sequence according to claim 107 wherein X_{21} is phenylalanine.

109. The amino acid sequence according to claim 103 wherein X_{15} is a large amino acid.

110. The amino acid sequence according to claim 101 wherein at least one amino acid is a D-amino acid.

111. The amino acid sequence according to claim 65 wherein at least one amino acid is a D-amino acid.

112. The amino acid sequence according to claim 102 wherein said amino acid sequence further comprises an amino acid extension comprising $X_{101}X_{102}X_{103}$ wherein X_{103} is bound to X_{14} at the amino terminus and X_{101} and X_{102} are polar amino acids and X_{103} is a hydrophobic amino acid.

113. The amino acid sequence according to claim 112 wherein X_{101} and X_{102} are independently aspartic acid or glutamic acid and X_{103} is leucine, isoleucine or valine.

114. An amino acid sequence which binds Site 1 of IGF-1R from mammalian cells such that binding to IR is at or below background, said sequence comprising $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

115. The amino acid sequence according to claim 114 wherein X_{14} and X_{17} are selected from the group consisting of leucine, isoleucine and valine; X_{18} is an aromatic amino acid; X_{20} is selected from group consisting of tyrosine and histidine; and X_{21} is selected from group consisting of phenylalanine and tyrosine.

116. A method of binding to Site 2 of IR from mammalian cells, said method comprising contacting said cells with an amino acid sequence comprising $X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}X_{28}X_{29}X_{30}X_{31}X_{32}X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}$ wherein X_{22}, X_{25}, X_{26}, X_{28}, X_{29}, X_{30}, X_{33}, X_{34}, X_{35}, X_{37}, X_{38}, X_{40} and X_{41} are any amino acid; X_{23} is any hydrophobic amino acid; X_{27} is a polar amino acid; X_{31} is an aromatic amino acid; X_{32} is a small amino acid; and wherein at least one cysteine is located at positions X_{24} through X_{27} and one at X_{39} or X_{40}.

117. The method according to claim 116 wherein X_{24} and X_{39} are cysteines.

118. The method according to claim 117 wherein X_{23} is selected from leucine, isoleucine, methionine and valine; X_{27} is selected from glutamic acid, aspartic acid, asparagine, and glutamine; X_{31} is tryptophan, X_{32} is glycine; and X_{36} is any aromatic amino acid.

119. The method according to claim 118 wherein the binding to IR occurs at an affinity (K_d) of at least about 10^{-5} M.

120. The method according to claim 116 wherein X_{23} is leucine, X_{27} is glutamic acid, X_{31} is tryptophan, and X_{32} is glycine.

121. (Once Amended) The method according to claim 116 wherein the amino acid sequence is HLCVLEELFWGASLFGYCSG (SEQ ID NO: 1509).

122. An amino acid sequence which binds IR, said amino acid sequence comprising
$X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}X_{28}X_{29}X_{30}X_{31}X_{32}X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}$
wherein X_{22}, X_{25}, X_{26}, X_{28}, X_{29}, X_{30}, X_{33}, X_{34}, X_{35}, X_{37}, X_{38}, X_{40} and X_{41} are any amino acid, X_{23} is any hydrophobic amino acid, X_{27} is a polar amino acid; X_{31} is an aromatic amino acid; X_{32} is a small amino acid, and wherein at least one cysteine is located at positions X_{24} through X_{27} and one at X_{39} or X_{40}.

123. The amino acid sequence according to claim 122 wherein X_{24} and X_{39} are cysteines.

124. The amino acid sequence according to claim 123 wherein X_{23} is selected from methionine, valine, and leucine; X_{27} is selected from glutamic acid, alanine, glycine, glutamine, aspartic acid and valine; X_{31} and X_{32} are small amino acids; and X_{36} is an aromatic amino acid.

125. The amino acid sequence according to claim 122 wherein the binding to IR occurs at an affinity (K_d) of at least about 10^{-5} M.

126. The amino acid sequence according to claim 124 wherein X_{23} is leucine, X_{27} is glutamic acid, X_{31} is tryptophan, and X_{32} is glycine.

127. (Once Amended) The amino acid sequence according to claim 122 wherein the amino acid sequence is HLCVLEELFWGASLFGYCSG (SEQ ID NO: 1509).

128. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence which binds IR and comprises the sequence X_{42} X_{43} X_{44} X_{45} X_{46} X_{47} X_{48} X_{49} X_{50} X_{51} X_{52} X_{53} X_{54} X_{55} $X_{56}X_{57}X_{58}X_{59}$ X_{60} X_{61} wherein X_{42}, X_{43}, X_{44}, X_{45}, X_{53}, X_{55}, X_{56}, X_{58}, X_{60} and X_{61} are any amino acid; X_{43}, X_{46}, X_{49}, X_{50} and X_{54} are hydrophobic amino acids; X_{47} and X_{59} are cysteines; X_{48} is a polar amino acid; X_{51}, X_{52} and X_{57} are small amino acids.

129. The method according to claim 128 wherein X_{43} and X_{46} are leucine; X_{48} is selected from the group consisting of aspartic acid and glutamic acid; X_{50} is phenylalanine or tyrosine; and X_{51} ,X_{52} and X_{57} are glycine.

130. The method according to claim 129 wherein X_{48} is glutamic acid and X_{50} is a phenylalanine.

131. (Once Amended) The method according to claim 130 wherein the amino acid sequence is X_{42} X_{43} X_{44} X_{45}LCE X_{49} FGG X_{53} X_{54} X_{55} X_{56}GX_{58}C X_{60} X_{61} (SEQ ID NO: 2422).

132. (Once Amended) The method according the claim 131 wherein the amino acid sequence comprises DLRVLCELFGGAYVLGYCSE (SEQ ID NO: 1732) or DLRVLCELFGGAYVRGYCSE (SEQ ID NO: 2642).

133. The method according to claim 128 wherein the binding to IR occurs at an affinity (K_d) of at least about 10^{-5} M.

134. An amino acid sequence which binds IR, said amino acid sequence comprising X_{42} X_{43} X_{44} X_{45} X_{46} X_{47} X_{48} X_{49} X_{50} X_{51} X_{52} X_{53} X_{54} X_{55} $X_{56}X_{57}X_{58}X_{59}$ X_{60} X_{61} wherein X_{42}, X_{43}, X_{44}, X_{45}, X_{53}, X_{55}, X_{60} and X_{61} are any amino acid; X_{43}, X_{46}, X_{49}, X_{50} and X_{54} are hydrophobic amino acids; X_{47} and X_{59} are cysteines; X_{48} is a polar amino acid; and X_{51} ,X_{52} and X_{57} are small amino acids.

135. The amino acid sequence according to claim 134 wherein X_{43} and X_{46} are leucine; X_{48} is selected from the group consisting of aspartic acid and glutamic acid; X_{50} is phenylalanine or tyrosine; and X_{51} ,X_{52} and X_{57} are glycine.

136. The amino acid sequence according to claim 135 wherein X_{48} is glutamic acid and X_{50} is phenylalanine.

137. (Once Amended) The amino acid sequence according to claim 136 wherein the amino acid sequence comprisesX_{43} X_{44} X_{45} LCE X_{49} FGG X_{53} X_{54} X_{55} X_{56} G X_{58} C X_{60} X_{61} (SEQ ID NO: 2422).

138. (Once Amended) The amino acid sequence according to claim 137 wherein an amino acid sequence comprisesDLRVLCELFGGAYVLGYCSE (SEQ ID NO: 1732) or DLRVLCELFGGAYVRGYCSE (SEQ ID NO: 2642).

139. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence comprising X_{62} X_{63} X_{64} X_{65} X_{66} X_{67} X_{68} X_{69} X_{70} X_{71} X_{72} X_{73} X_{74} X_{75} X_{76} X_{77} X_{78} X_{79} X_{80} X_{81} wherein X_{62}, X_{65}, X_{66} X_{68}, X_{69}, X_{71}, X_{73}, X_{76}, X_{77}, X_{78}, X_{80} and X_{81} are any amino acid; X_{63}, X_{70}, and X_{74} are hydrophobic amino acids; X_{64} is a polar amino acid; X_{67} and X_{75} are aromatic amino acids; and X_{72} and X_{79} are cysteines.

140. The method according to claim 139 wherein X_{63} is selected from the group consisting of leucine, isoleucine, methionine and valine; X_{70} and X_{74} are selected from group consisting of valine, isoleucine, leucine and methionine; X_{64} is selected from group consisting of aspartic acid and glutamic acid; X_{67} is tryptophan; and X_{75} is selected from group consisting of tyrosine and tryptophan.

141. The method according to claim 140 wherein X_{66} is glutamic acid.

142. The method according to claim 141 wherein X_{63} is leucine.

143. The method according to claim 140 wherein X_{74} is valine.

144. The method according to claim 141 wherein X_{64} is a glutamic acid.

145. The method according to claim 141 wherein X_{75} is a tyrosine.

146. (Once Amended) The method accord to claim 140 wherein the amino acid sequence comprises WLDQEWAWVQCEVYGRGCPS (SEQ ID NO: 1735).

147. An amino acid sequence which binds IR, said amino acid sequence comprising X_{62} X_{63} X_{64} X_{65} X_{66} X_{67} X_{68} X_{69} X_{70} X_{71} X_{72} X_{73} X_{74} X_{75} X_{76} X_{77} X_{78} X_{79} X_{80} X_{81} wherein X_{62}, X_{65}, X_{66} X_{68}, X_{69}, X_{71}, X_{73}, X_{76}, X_{77}, X_{78}, X_{80} and X_{81} are any amino acid; X_{63}, X_{70}, and X_{74} are hydrophobic amino acids; X_{64} is a polar amino acid; X_{67} and X_{75} are aromatic amino acids; and X_{72} and X_{79} are cysteines.

148. The amino acid sequence according to claim 147 wherein X_{63} is selected from the group consisting of leucine, isoleucine, methionine and valine; X_{70} and X_{74} are selected from group consisting of valine, isoleucine, leucine and methionine; X_{64} is selected from group consisting of aspartic acid and glutamic acid; X_{67} is tryptophan; and X_{75} is selected from group consisting of tyrosine and tryptophan.

149. The amino acid sequence according to claim 148 wherein X_{66} is glutamic acid.

150. The amino acid sequence according to claim 149 wherein X_{63} is leucine.

151. The amino acid sequence according to claim 148 wherein X_{74} is valine.

152. The amino acid sequence according to claim 149 wherein X_{64} is glutamic acid.

153. The amino acid sequence according to claim 148 wherein X_{75} is a tyrosine.

154. (Once Amended) The amino acid sequence accord to claim 148 wherein the amino acid sequence comprises WLDQEWAWVQCEVYGRGCPS (SEQ ID NO: 1735).

155. The amino acid sequence according to claim 148 wherein the affinity (K_d) of binding to IR is at least 10^{-5} M.

156. The amino acid sequence according to claim 148 wherein the amino acid sequence comprises a sequence selected from the sequences of Figures 6A-6F.

157. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence which binds IR and comprises $HX_{82}X_{83}X_{84}X_{85}X_{86}X_{87}X_{88}X_{89}X_{90}X_{91}X_{92}$ herein X_{82} is proline or alanine; X_{83} is a small amino acid; X_{84} is selected from the group consisting of leucine, serine and threonine; X_{85} is a polar amino acid; X_{86} is any amino acid; X_{87} is an aliphatic amino acid; X_{88}, X_{89}, X_{90} is any amino acid; and X_{91} and X_{92} are aliphatic amino acids.

158. The method according to claim 157 wherein X_{82} is proline; X_{83} is selected from the group consisting of proline, serine and threonine; X_{84} is leucine; X_{85} is selected from the group consisting of glutamic acid, serine, lysine and asparagine; X_{86} is a polar amino acid; X_{87} is selected from the group consisting of leucine, methionine and isoleucine; and X_{91} and X_{92} are leucines.

159. The method according to claim 158 wherein X_{83} is proline.

160. The method according to claim 158 wherein X_{85} is serine.

161. The method according to claim 158 wherein X_{86} is selected from the group consisting of histidine, glutamic acid, aspartic acid and glutamine.

162. The method according to claim 158 wherein X_{87} is leucine.

163. The method according to claim 158 wherein X_{92} is phenylalanine.

164. (Once Amended) The method according to claim 160 wherein the amino acid sequence is HPPLSX_{86} LX_{88} X_{89} X_{90} LL (SEQ ID NO: 2424).

165. (Once Amended) The method according to claim 158 wherein the amino acid sequence is selected from the group consisting of HPPLEHLKAFLL (SEQ ID NO: 1869), HPPLSELKLFLI (SEQ ID NO: 2643), HPSLSDMRWILL (SEQ ID NO: 2644), HPTSKEIYAKLL (SEQ ID NO: 2645), HPTSKEIYAKLL (SEQ ID NO: 2645), HPSTNQMLMKLF (SEQ ID NO: 2646) and HAPLSVLQALL (SEQ ID NO: 2647).

166. An amino acid sequence which binds IR, said amino acid sequence comprising H$X_{82}X_{83}X_{84}X_{85}X_{86}X_{87}X_{88}X_{89}X_{90}X_{91}X_{92}$ herein X_{82} is proline or alanine; X_{83} is a small amino acid; X_{84} is selected from the group consisting of leucine, serine and threonine; X_{85} is a polar amino acid; X_{86} is any amino acid; X_{87} is an aliphatic amino acid; X_{88}, X_{89}, X_{90} is any amino acid; and X_{91} and X_{92} are aliphatic amino acids.

167. The amino acid sequence according to claim 166 wherein X_{82} is proline; X_{83} is selected from the group consisting of proline, serine and threonine; X_{84} is leucine; X_{85} is selected from the group consisting of glutamic acid, serine, lysine and asparagine; X_{86} is a polar amino acid; X_{87} is selected from the group consisting of leucine, methionine and isoleucine; and X_{91} and X_{92} are leucines.

168. The amino acid sequence according to claim 167 wherein X_{83} is proline.

169. The amino acid sequence according to claim 167 wherein X_{85} is serine.

170. The amino acid sequence according to claim 167 wherein X_{86} is selected from the group consisting of histidine, glutamic acid, aspartic acid and glutamine.

171. The amino acid sequence according to claim 167 wherein X_{87} is leucine.

172. The amino acid sequence according to claim 167 wherein X_{92} is phenylalanine.

173. (Once Amended) The amino acid sequence according to claim 169 wherein the amino acid sequence is HPPLSX_{86} LX_{88} X_{89} X_{90} LL (SEQ ID NO: 2424).

174. (Once Amended) The amino acid sequence according to claim 167 wherein the amino acid sequence is selected from the group consisting of HPPLEHLKAFLL (SEQ ID NO: 1869), HPPLSELKLFLI (SEQ ID NO: 2643), HPSLSDMRWILL (SEQ ID NO: 2644), HPTSKEIYAKLL (SEQ ID NO: 2645), HPTSKEIYAKLL (SEQ ID NO: 2645), HPSTNQMLMKLF (SEQ ID NO: 2646) and HAPLSVLQALL (SEQ ID NO: 2647).

175. A method modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence comprising an amino acid sequence of $X_{104}X_{105}X_{106}X_{107}X_{108}X_{109}X_{110}X_{111}X_{112}X_{113}X_{114}$ wherein at least one of the amino acids of X_{106} through X_{111} are tryptophan; wherein X_{104} and X_{114} are both small amino acids; wherein X_{105} is any amino acid; and wherein at least one of X_{104}, X_{105}, X_{106} and one of X_{112} X_{113} X_{114} are cysteine residues.

176. The method according to claim 175 wherein at least two of the amino acids of X_{106} through X_{111} are tryptophan which are separated from each other by at least two amino acids.

177. The method according to claim 176 wherein the separating amino acids are selected from the group consisting of proline, threonine and tyrosine.

178. (Once Amended) The method according to claim 177 wherein the amino acid sequence comprises WPTYW (SEQ ID NO: 2425).

179. The method according to claim 178 wherein X_{105} and X_{113} are cysteine residues.

180. The method according to claim 178 wherein X_{104} and X_{114} are selected from the group consisting of alanine and glycine.

181. The method according to claim 180 wherein X_{104} is alanine and X_{114} is glycine.

182. The method according to claim 181 wherein X_{105} is valine.

183. The method according to claim 182 wherein X_{112} is asparagine.

184. The method according to claim 198 wherein the affinity (K_d) of binding to IR is at least about 10^{-5} M.

185. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence comprising an amino acid sequence selected from the group listed in Figure 8.

186. (Once Amended) The method according to claim 185 wherein the sequence comprises ACVWPTYWNCG (SEQ ID NO: 1874).

187. An amino acid sequence which binds and IR and comprising an amino acid sequence of $X_{104}X_{105}X_{106}X_{107}X_{108}X_{109}X_{110}X_{111}X_{112}X_{113}X_{114}$ wherein at least one of the amino acids of X_{106} through X_{111} are tryptophan; wherein X_{104} and X_{114} are both small amino acids; wherein X_{105} is any amino acid; and wherein at least one of X_{104}, X_{105}, X_{106} and one of X_{112} X_{113} X_{114} are cysteine residues.

188. The amino acid sequence according to claim 187 wherein at least two of the amino acids of X_{106} through X_{111} are tryptophan which are separated from each other by at least two amino acids.

189. The amino acid sequence according to claim 188 wherein the separating amino acids are selected from the group consisting of proline, threonine and tyrosine.

190. (Once Amended) The amino acid sequence according to claim 189 wherein the amino acid sequence comprises WPTYW (SEQ ID NO: 2425).

191. The amino acid sequence according to claim 190 wherein X_{105} and X_{113} are cysteine residues.

192. The amino acid sequence according to claim 190 wherein X_{104} and X_{114} are selected from the group consisting of alanine and glycine.

193. The amino acid sequence according to claim 190 wherein X_{104} is alanine and X_{114} is glycine.

194. The amino acid sequence according to claim 193 wherein X_{105} is valine.

195. The amino acid sequence according to claim 194 wherein X_{112} is asparagine.

196. The amino acid sequence according to claim 202 wherein the affinity (K_d) of binding to IR is at least about 10^{-5} M.

197. An amino acid sequence which binds IR from mammalian cells comprising an amino acid sequence selected from the group listed in Figure 8.

198. (Once Amended) The amino acid sequence according to claim 197 comprising ACVWPTYWNCG (SEQ ID NO: 1874).

199. (Once Amended) A method of providing insulin agonist activity to mammalian cells, said method comprising administering to said cells an amino acid sequence comprising DYKDLCQSWGVRIGWLAGLCPKK (SEQ ID NO: 2152).

200. A method of modulating insulin activity in mammalian cells, said method comprising administering to said cells an amino acid sequence comprising an amino acid sequence selected from the group listed in Figures 9 through 11.

201. (Once Amended) An amino acid sequence comprising DYKDLCQSWGVRIGWLAGLCPKK (SEQ ID NO: 2152).

202. An amino acid sequence comprising an amino acid sequence selected from the group listed in Figures 9 through 11.

203. An amino acid sequence comprising at least two amino acid sequences which independently bind IR, with the proviso that at least one of the sequences is not insulin or a fragment thereof.

204. The amino acid sequence according to claim 203 wherein the two amino acid sequences bind to Site 1 of IR.

205. The amino acid sequence according to claim 203 wherein one amino acid sequence binds to Site 1, and the other binds to Site 2 of IR.

206. The amino acid sequence according to claim 203, wherein at least one of the sequences is selected from the group consisting of $X_1X_2X_3X_4X_5$ wherein X_1, X_2, X_4, and X_5 are aromatic amino acids, and X_3 may be any polar amino acid; $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ wherein X_6 and X_7 are aromatic amino acids or glutamine, X_8, X_9, X_{11} and X_{12} may be any amino acid, X_{10} and X_{13} are hydrophobic amino acids; and $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

207. The amino acid sequence according to claim 206, wherein at least one of the sequences is $X_1X_2X_3X_4X_5$ wherein X_1, X_2, X_4, and X_5 are aromatic amino acids, and X_3 may be any polar amino acid.

208. (Once Amended) The amino acid sequence according to claim 206 wherein at least one of the sequences comprises FYX_3WF (SEQ ID NO: 2415).

209. The amino acid sequence according to claim 206, wherein at least one of the sequences comprises $X_6X_7X_8X_9X_{10}X_{11}X_{12}X_{13}$ wherein X_6 and X_7 are aromatic amino acids or glutamine, X_8, X_9, X_{11} and X_{12} may be any amino acid, X_{10} and X_{13} are hydrophobic amino acids.

210. (Once Amended) The amino acid sequence according to claim 209, wherein at least one of the sequences comprises $FYX_8X_9LX_{11}X_{12}L$ (SEQ ID NO: 2416).

211. The amino acid sequence according to claim 206, wherein at least one of the sequences comprises $X_{14}X_{15}X_{16}X_{17}X_{18}X_{19}X_{20}X_{21}$ wherein X_{14}, X_{17}, and X_{18} are hydrophobic amino acids, X_{15}, X_{16}, and X_{19} are any amino acid, and X_{20} and X_{21} are aromatic amino acids.

212. (Once Amended) The amino acid sequence according to claim 211 wherein at least one of the sequences comprises LX_{15}, X_{16}, $LLX_{19}YF$ (SEQ ID NO: 2648).

213. The amino acid sequence according to claim 203 wherein at least one of the sequences comprises $X_{22}X_{23}X_{24}X_{25}X_{26}X_{27}X_{28}X_{29}X_{30}X_{31}X_{32}X_{33}X_{34}X_{35}X_{36}X_{37}X_{38}X_{39}X_{40}X_{41}$ wherein X_{22}, X_{25}, X_{26}, X_{28}, X_{29}, X_{30}, X_{33}, X_{34}, X_{35}, X_{36}, X_{37}, X_{38}, X_{40}, and X_{41} are any amino acid, X_{23} is any hydrophobic amino acid; X_{27} is a polar amino acid; X_{31} is an aromatic amino acid; X_{32} is a small amino acid, and wherein at least one cysteine is located at positions X_{24} through X_{27} and one at X_{39} or X_{40}; X_{42} X_{43} X_{44} X_{45} X_{46} X_{47} X_{48} X_{49} X_{50} X_{51} X_{52} X_{53} X_{54} X_{55} $X_{56}X_{57}X_{58}X_{59}$ X_{60} X_{61} wherein X_{42}, X_{43}, X_{44}, X_{45}, X_{53}, X_{55}, X_{56}, X_{58}, X_{60} and X_{61} are any amino acid; X_{43}, X_{46}, X_{49}, X_{50} and X_{54} are hydrophobic amino acids; X_{47} and X_{59} are cysteine; X_{48} is a polar amino acid; and X_{51} ,X_{52} and X_{57} are small amino acids; or X_{62} X_{63} X_{64} X_{65} X_{66} X_{67} X_{68} X_{69} X_{70} X_{71} X_{72} X_{73} X_{74} X_{75} X_{76} X_{77} X_{78} X_{79} X_{80} X_{81} wherein X_{62}, X_{65}, X_{66} X_{68}, X_{69}, X_{71}, X_{73}, X_{76}, X_{77}, X_{78}, X_{80} and X_{81} are any amino acid; X_{63}, X_{70}, and X_{74} are hydrophobic amino acids; X_{64} is a polar amino acid; X_{67} and X_{75} are aromatic amino acids; and X_{72} and X_{79} are cysteines.

214. The amino acid sequence according to claim 203 wherein at least one of the sequences comprises $HX_{82}X_{83}X_{84}X_{85}X_{86}X_{87}X_{88}X_{89}X_{90}X_{91}X_{92}$ herein X_{82} is proline or alanine; X_{83} is a small amino acid; X_{84} is selected from the group consisting of leucine, serine and threonine; X_{85} is a polar amino acid; X_{86} is any amino acid; X_{87} is an aliphatic amino acid; X_{88}, X_{89}, X_{90} is any amino acid; and X_{91} and X_{92} are aliphatic amino acids or $X_{104}X_{105}X_{106}X_{107}X_{108}X_{109}X_{110}X_{111}X_{112}X_{113}X_{114}$ wherein at least one of the amino acids of X_{106} through X_{111} are tryptophan; wherein X_{104} and X_{114} are both small amino acids; wherein X_{105} is any amino acid; and wherein at least one of X_{104}, X_{105}, X_{106} and one of X_{112} X_{113} X_{114} are cysteine residues.

215. The amino acid sequence according to claim 203 wherein the two amino acid sequences are connected by a peptide or non-peptide linker.

216. The amino acid sequence according to claim 215 wherein the linker is a peptide consisting of about 2 to about 16 amino acids.

217. The amino acid sequence according to claim 215 wherein the linker is a non-peptide.

218. The amino acid sequence according to claim 217 wherein the linker is dialdehyde.

219. (Once Amended) The amino acid sequence according to claim 203 wherein the amino acid sequence is selected from the group consisting of

DYKDDDDKFHENFYDWFVRQVSGSGSGLDALDRLMRYGEERPSLA AAGAP (SEQ ID NO: 2649),

DYKDDDDKFHENFYDWFVRQVSGGSHLCVLEELFWGASLFGYCSG AAAGAPVPYPDPLEPRAA (SEQ ID NO: 2619),

DYKDDDDKFHENFYDWFVRQVSGGSGGSGGSHLCVLEELFWGASL FGYCSGAAAGAPVPYPDPLEPRAA (SEQ ID NO: 2620),

DYKDDDDKFHENFYDWFVRQVSGGSGGSGGSGGSHLCVLEELFWG ASLFGYCSGAAAGAPVPYPDPLEPRAA (SEQ ID NO: 2621),

AQPAMAFHENFYDWFVRQVSGGSFHENFYDWFVRQVSAAAGAPVP YPDPLEPRAA (SEQ ID NO: 2627),

AQPAMAFHENFYDWFVRQVSGGSFHENFYDWFVRQVSGGSFHENF YDWFVRQVSAAAGAPVPYPDPLEPRAA (SEQ ID NO: 2628),

AQPAMAFHENFYDWFVRQVSGGSGGSFHENFYDWFVRQVSAAAG APVPYPDPLEPRAA (SEQ ID NO: 2629),

AQPAMAFHENFYDWFVRQVSGGSGGSGGSFHENFYDWFVRQVSAA AGAPVPYPDPLEPRAA (SEQ ID NO: 2630) and

AQPAMAFHENFYDWFVRQVSGGSGGSGGSGGSFHENFYDWFVRQV SAAAGAPVPYPDPLEPRAA (SEQ ID NO: 2631).

220. A nucleic acid sequence encoding amino acid sequence which binds to IR at Site 1 and/or Site 2, with the proviso that the sequence is not insulin, IGF, or fragments thereof.

221. (Once Amended) The nucleic acid sequence according to claim 220 wherein the nucleic acid sequence encodes for an amino acid sequence selected from the group consisting of FYDWF (SEQ ID NO: 2411), FYEWF (SEQ ID NO: 2412), FHENFYDWF (SEQ ID NO: 2635), FHENFYDWFVRQVSK (SEQ ID NO: 2115), DYKDVTFTSAVFHENFYDWFVRQVSKK (SEQ ID NO: 2111), GRVDWLQRNANFYDWFVAELG (SEQ ID NO: 2163) and APTFYAWFNQQT (SEQ ID NO: 1870).

222. (Once Amended) The nucleic acid sequence according to claim 220 wherein the nucleic acid sequence encodes for an amino acid sequence selected from the group consisting of DYKDFYDAIDQLVRGSARAGGTRDKK (SEQ ID NO: 2116) and KDRAFYNGLRDLVGAVYGAWDKK (SEQ ID NO: 2117).

223. (Once Amended) The nucleic acid sequence according to claim 220 wherein the nucleic acid sequence encodes for an amino acid sequence selected from the group consisting of SFYEAIHQLLGV (SEQ ID NO: 1964),

NSFYEALRMLSS (SEQ ID NO: 2638),
SLNFYDALQLLA (SEQ ID NO: 2639),
SSNFYQALMLLS (SEQ ID NO: 2471),
SDGFYNAIELLS (SEQ ID NO: 2460),
HETFYSMIRSLA (SEQ ID NO: 2640),
HDPFYSMMKSLL (SEQ ID NO: 2641) and
WSDFYSYFQGL (SEQ ID NO: 2650).

224. A kit for identifying a compound which binds IGF-1 receptor, comprising a IGF-1 receptor and an amino acid sequence selected from Formulas 1-10, or the amino acid sequences of Figures 9-11, which bind to the receptor at Site 1 or Site 2.

225. (Once Amended) The kit according to claim 224, wherein the amino acid sequence comprises the amino acid sequence FYDWF (SEQ ID NO: 2411).

226. (Once Amended) The kit according to claim 225, wherein the amino acid sequence comprises the amino acid sequence SAKNFYDWFVKK (SEQ ID NO: 2112).

227. (Once Amended) The kit according to claim 226 wherein the amino acid sequence comprises the amino acid sequence FYSLLASL (SEQ ID NO: 2651).

228. (Once Amended) The kit according to claim 227 wherein the amino acid sequence comprises the amino acid sequence QMKDIFYSLLASLAAKK (SEQ ID NO: 2652).

229. A kit for identifying a compound which binds IR comprising IR and an amino acid sequence selected from Formulas 1-10 or the amino acid sequences of Figures 9 and 11 which bind IR at Site 1 or Site 2.

230. A pharmaceutical composition comprising a amino acid sequence which binds specifically to IGF-1 receptor at Site 1 and is an IGF agonist, with the proviso that the amino acid sequence is not IGF-1, insulin, or fragments thereof, and a pharmaceutically acceptable carrier.

231. (Once Amended) The composition according to claim 230, wherein the peptide comprises the amino acid sequence NFYDWFV (SEQ ID NO: 2435).

232. (Once Amended) The pharmaceutical composition according to claim 230, wherein the peptide comprises the amino acid sequence QMKDIFYSLLASLAA (SEQ ID NO: 2653).

233. A pharmaceutical composition comprising a amino acid sequence which binds specifically to IR receptor at Site 1and is an insulin agonist, with the proviso that the amino acid sequence is not insulin, IGF, or fragments thereof, and a pharmaceutically acceptable carrier.

234. (Once Amended) The pharmaceutical composition according to claim 233, wherein the peptide comprises the amino acid sequence FYDWF (SEQ ID NO: 2411).

235. (Once Amended) The pharmaceutical composition according to claim 233, wherein the peptide comprises the amino acid sequence FYSLLASL (SEQ ID NO: 2651).

236. A method of treating diabetes comprising administering to an individual in need of treatment a therapeutically effective amount of an amino acid sequence which binds IR at Site 1 and is an insulin agonist, with the proviso that the amino acid sequence is not insulin, IGF, or fragments thereof.

237. The method according to claim 236 wherein the amino acid sequence is expressed by a recombinant vector administered to the individual.

238. The method according to claim 236 wherein the amino acid sequence is administered to the individual as a polypeptide.

239. A method of treating a patient with an IGF sensitive tumor comprising administering to an individual in need of treatment a therapeutically effective amount of an amino acid sequence which is an IGF-1R antagonist, with the proviso that the amino acid sequence is not insulin, IGF, or fragments thereof.

240. The method according to claim 239 wherein the amino acid sequence is expressed by a recombinant vector administered to the individual.

241. The method according to claim 239 wherein the amino acid sequence is administered to the individual as a polypeptide.

242. A method of screening for a compound which binds to IR comprising:

i) immobilizing IR, or a fragment thereof, on a surface;

ii) incubating the IR, or fragment thereof, with a known amount of labeled amino acid sequence of Formulas 1-10, or an amino acid sequence selected from Figures 10-11, which binds IR and a compound to be screened under conditions which provide for binding of the labeled amino acid sequence to bind IR;

iii) measuring the amount of labeled amino acid sequence bound to IR;

iv) determining from the amount of bound labeled peptide whether the compound has competitively bound to IR.

243. An amino acid sequence capable of binding to Site 1 or Site 2 of IR identified by the method according to claim 242, with the proviso that the amino acid sequence is not insulin, IGF, or fragments thereof.

244. The amino acid sequence according to claim 243 wherein the amino acid sequence is an IR agonist.

245. The amino acid sequence according to claim 243 wherein the amino sequence binds to Site 1 of IR.

246. The amino acid sequence according to claim 243 wherein the amino sequence binds to Site 2 of IR.

247. A method of screening for a compound which binds to IGF-1R comprising:

i) immobilizing IGF-1R, or a fragment thereof, on a surface;

ii) incubating the IGF-1R, or fragment thereof, with a known amount of labeled amino acid sequence of Formulas 1-9, or an amino acid sequence selected from Figure 10, which binds IGF-1R and a compound to be screened under conditions which provide for binding of the labeled amino acid sequence to bind to IGF-1R;

iii) measuring the amount of labeled amino acid sequence bound to IGF-1R;

iv) determining from the amount of bound labeled peptide whether the compound has competitively bound to IGF-1R.

248. An amino acid sequence capable of bind to Site 1 or Site 2 of IGF-1R identified by the method according to claim 247, with the proviso that the amino acid sequence is not insulin, IGF, or fragments thereof.

249. The amino acid sequence according to claim 248 wherein the amino acid sequence is an IGF agonist.

250. The amino acid sequence according to claim 248 wherein the amino sequence binds to Site 1 of IGF-1R.

251. The amino acid sequence according to claim 248 wherein the amino sequence binds to Site 2 of IGF-1R.

252. (Once Amended) An amino acid sequence comprising the sequence $WX_{123}GYX_{124}WX_{125}X_{126}$ (SEQ ID NO: 2414) wherein X_{123} is proline, glycine, serine, arginine, alanine or leucine, X_{124} is any amino acid; X_{125} is a hydrophobic amino acid; and X_{126} is any amino acid.

253. The amino acid sequence according to claim 252 wherein X_{123} is proline and X_{125} is leucine or phenylalanine.

254. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 1.

255. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 2.

256. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 3.

257. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 4.

258. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 5.

259. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 6.

260. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 7.

261. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 8.

262. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 9.

263. A recombinant peptide library comprising members wherein the majority of the members comprise an amino acid sequence of Formula 10.